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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

RABIES PROPHYLAXIS

INTRODUCTION

Although human rabies is rare in the United States, thousands of persons receive rabies prophylaxis each year. Management of those who possibly have been exposed to rabies infection is of paramount importance. The following is a current interpretation both of the risk of infection and the efficacy of treatment. It incorporates many basic concepts of the World Health Organization Expert Committee on Rabies.

The problem of whether or not to immunize those bitten, scratched, or otherwise exposed to rabies by animals suspected of being infectious is a perplexing one for physicians. All available methods of systemic treatment are complicated by instances of adverse reactions, a few of which have resulted in death or permanent disability. Furthermore, decisions on management must be made immediately, because the longer treatment is postponed, the less likely it is to be effective.

Data on the efficacy of active and passive immunization after rabies exposure have come principally from studies in animals. Because rabies has occasionally developed in humans who had received antirabies prophylaxis, the data have been questioned. Evidence from laboratory and field experience in many areas of the world, however, indicates that post-exposure prophylaxis is usually effective when appropriately used.

Rabies in the United States

Rabies in humans has decreased from an average of 22 cases per year in 1946–1950 to only 1 or 2 cases per year since 1963. Rabies in domestic animals has diminished similarly. In 1946, for example, there were more than 8,000 cases of rabies in dogs, compared with 230 in 1971. Thus, the likelihood of humans being exposed to rabies by domestic animals has decreased greatly; although bites by dogs and cats continue to be responsible for the overwhelming majority of antirabies treatments.

In contrast, the disease in wildlife–especially skunks, foxes, raccoons, and bats–has become increasingly prominent in recent years, accounting for more than 70 percent of all reported cases of animal rabies in 1971. Wild animals constitute the most important source of infection for man and domestic animals in the United States today. In 1971, only a single State reported no wildlife rabies.

Antirabies Treatment in the United States

More than 30,000 persons receive post-exposure antirabies treatment each year. However, there is no information on the number of persons actually exposed to rabid animals.

In the United States, nervous tissue origin rabies vaccine of the Semple type (NTV) was used almost exclusively until 1957, when duck embryo origin vaccine (DEV) was licensed. More than 90 percent of those who received rabies prophylaxis in the United States in 1971 were given DEV.

RABIES VACCINES

Duck Embryo Vaccine (DEV)

Prepared from embryonated duck eggs infected with a fixed virus and inactivated with beta-propiolactone.

Nervous Tissue Vaccine (NTV)

Prepared from rabbit brain infected with a fixed virus and inactivated with phenol (Semple type) or inactivated with ultraviolet irradiation.

Antigenicity of Vaccines

The antigenicity of NTV is often higher than that of DEV when tested in experimental animals. However, all lots of both vaccines must pass minimum potency tests established by the Division of Biologics Standards. There is evidence that the serum antibody response in humans is detectable sooner with DEV, but the eventual level of response is frequently higher with NTV.

Effectiveness of Vaccines in Humans

In the United States, comparative effectiveness of vaccines can be judged only by reported failures. During the years 1957 through 1971 when both vaccines were available, there were 6 rabies deaths among the 125,000 NTV-treated persons (1:20,800) and 12 among the 310,000 treated with DEV (1:25,800).

Reactions

Erythema, pruritus, pain, and tenderness at the site of inoculation are common with both DEV and NTV. Systemic responses, including low-grade fever or rarely shock, may occasionally occur late in the course of therapy with either vaccine, usually after 5–8 doses. In rare instances, serious reactions have occurred after the first dose of DEV or NTV, particularly in persons previously sensitized with vaccines containing avian or rabbit brain tissue.

Neuroparalytic reactions occur rarely with DEV. They much more frequently follow NTV, especially after repeated courses of treatment with this preparation.

Choice of Vaccine

Treatment-failure rates for the 2 vaccines are not significantly different; therefore, the lower incidence of central nervous system reactions with DEV makes it preferable to NTV.

RATIONALE OF TREATMENT

Every exposure to possible rabies infection must be individually evaluated.

In the United States, the following factors should be considered before specific antirabies treatment is initiated:

Species of Biting Animal

Carnivorous animals (especially skunks, foxes, coyotes, raccoons, dogs, and cats) and bats are more likely to be infective than other animals. Bites of rabbits, squirrels, chipmunks, rats, and mice, seldom, if ever, call for rabies prophylaxis.

Circumstances of Biting Incident

An UNPROVOKED attack is more likely to mean that the animal is rabid. (Bites during attempts to feed or handle an apparently healthy animal should generally be regarded as PROVOKED.)

Type of Exposure

Rabies is transmitted by inoculation of infectious saliva through the skin. Thus, the likelihood that rabies infection will result from exposure to a rabid animal varies with the nature and extent of the exposure. Two categories of exposure should be considered:

Bite wounds: any penetration of the skin by teeth.

Non-bite wounds: scratches, abrasions, or open wounds.

Vaccination Status of Biting Animal

A properly immunized animal has only a minimal chance of developing rabies and transmittting the virus.

Presence of Rabies in Region

If adequate laboratory and field records indicate that there is no rabies infection in a domestic species within a given region, local health officials are justified in considering this in recommendations on antirabies treatment following a bite by that particular species.

MANAGEMENT OF BITING ANIMALS

A healthy domestic dog or cat that bites a person should be captured, confined, and observed by a veterinarian for 10 days. (The commonly used 5–7 day observation period may not always be adequate.) Any illness in the animal should be reported immediately to the local health department.

If the dog or cat develops signs suggestive of rabies, the animal should be sacrificed and the head removed and shipped under refrigeration to a qualified laboratory designated by the local or State health department for examination.

Early signs of rabies in wild or stray animals cannot be interpreted reliably; therefore, any such animal that bites or scratches a person should be killed at once (without unnecessary damage to the head) and the brain examined for evidence of rabies.

If examination of the brain by fluorescent antibody technique is negative for rabies, the bitten person need not be treated.

LOCAL TREATMENT OF WOUNDS

Immediate and thorough local treatment of all bite wounds and scratches is perhaps the most effective means of preventing rabies. Experimentally, the incidence of rabies in animals can be markedly reduced by local therapy alone.

First-Aid Treatment to be Carried Out Immediately

Copious flushing with soap and water.

Treatment By or Under Direction of Physician

1. Thorough flushing and cleansing into the wound with soap solution. Quaternary ammonium compounds may also be used.*

2. If antirabies serum is indicated, (See Passive Immunization), up to one-half of the total dose should be thoroughly infiltrated around the wound. As in all instances when horse serum is to be used, a careful history should be taken and tests for hypersensitivity performed.

3. Tetanus prophylaxis and measures to control bacterial infection, as indicated.

POST-EXPOSURE PROPHYLAXIS

The following recommendations are intended only as a guide. They may be modified according to knowledge of the species of biting animal, circumstances surrounding the biting incident, vaccination status of the animal, and presence of rabies in the region.

Active Immunization

Vaccine without serum: 14 daily injections of the vaccine in the dose recommended by the manufacturer.

Vaccine with serum: When serum is used, 21 doses of vaccine are recommended. These may be given as 21 daily doses or 14 doses in the first 7 days (either as 2

*Such as Zephiran (Benzyl ammonium chloride). All traces of soap should be removed before applying quaternary ammonium compounds because soap neutralizes their activity.

separate injections or a double dose), and then 7 daily doses. Two booster doses, the first 10 days and the second at least 20 days after completion of the primary course, are necessary to assure lasting protection.

Precautions: Vaccine should be given subcutaneously in the abdomen, lower back, or lateral aspect of thighs; rotation of sites is recommended. Local reactions are common and do not contraindicate continuing treatment.

When rabies vaccine must be given to a person with a history of hypersensitivity, especially to avian or rabbit tissues, antihistaminic drugs may be given. Epinephrine is indicated in reactions of the anaphylactoid type. If serious allergic manifestations preclude continuation of prophylaxis with one vaccine, the other may be used.

If meningeal or neuroparalytic reactions develop, vaccine treatment should be discontinued altogether. Corticosteroids may interfere with development of active immunity and should only be used to treat neuroparalytic reactions.

Passive Immunization

Hyperimmune serum has proved effective in preventing rabies. Its use in combination with vaccine is considered the best post-exposure prophylaxis. However, the only preparation of antirabies serum currently available in the United States is of equine origin. Because horse serum has induced serum sickness in at least 20 percent of those who have received it, it should be used only when indicated.

Hyperimmune serum is recommended for ALL BITES by animals in which rabies cannot be excluded and for non-bite exposure to animals proven or suspect to be rabid (see accompanying guide). When indicated, antirabies serum should be used regardless of the interval between exposure and treatment.

The recommended dose of equine antirabies serum is 40 IU/kg, i.e., approximately 20 IU/lb or 1000 IU (1 vial)/55 pounds. Up to 50 percent of the antiserum should be used to infiltrate the wound and the rest administered intramuscularly. As previously noted, when using serum, a careful history must be obtained and appropriate tests for hypersensitivity performed.

PRE-EXPOSURE PROPHYLAXIS

The relatively low frequency of reactions to DEV has made it practical to offer pre-exposure immunization to persons in high-risk groups: veterinarians, animal handlers, certain laboratory workers, and individuals, especially children, living in areas of the world where rabies is a constant threat. Others whose vocational or avocational pursuits result in frequent contact with dogs, cats, foxes, skunks, or bats should also be considered for pre-exposure prophylaxis.

Two 1.0 ml injections of DEV given subcutaneously in the deltoid area 1 month apart should be followed by

POST-EXPOSURE ANTIRABIES GUIDE

The following recommendations are only a guide. They should be used in conjunction with knowledge of the animal species involved, circumstances of the bite or other exposure, vaccination status of the animal, and presence of rabies in the region.

Animal and Its Condition			Treatment	
Species		Condition at Time of Attack	Kind of Exposure	
			Bite*	Non-Bite*
Wild	Skunk Fox Raccoon Bat	Regard as Rabid	S + V[1]	S + V[1]
Domestic	Dog	Healthy	None[2]	None[2]
		Escaped (unknown)	S + V	V[3]
	Cat	Rabid	S + V[1]	S + V[1]
Other		Consider individually – See "Rationale of Treatment"		

* See text definitions
V Rabies Vaccine
S Antirabies Serum
1 Discontinue vaccine if fluorescent antibody (FA) tests of animal killed at time of attack are negative
2 Begin S + V at first sign of rabies in biting dog or cat during holding period (10 days)
3 14 Doses of DEV

a third dose 6–7 months after the second dose. This series of 3 injections can be expected to produce neutralizing antibody in 80–90 percent of vaccinees by 1 month after the third dose.

For more rapid immunization, 3 injections of DEV, 1.0 ml each, should be given at weekly intervals with a fourth dose 3 months later. This schedule elicits an antibody response in about 80 percent of the vaccinees.

All who receive the pre-exposure vaccination should have serum tested for neutralizing antibody 3–4 weeks after the last injection. Tests for rabies antibody can be arranged by State health department laboratories. If no antibody is detected, booster doses should be given until a response is demonstrated. Persons with continuing exposure should receive 1.0 ml boosters every 2–3 years.

When an immunized person with previously demonstrated rabies antibody is bitten by a rabid animal, it is suggested that he receive 5 daily doses of vaccine plus a booster dose 20 days later. Antirabies serum is not necessary in this case and, in fact, might inhibit a rapid anamnestic response. For non-bite exposures, an immunized person with antibody needs only a single dose of vaccine. If it is not known whether an exposed person ever had antibody, the complete post-exposure antirabies treatment should be given.

ACCIDENTAL INOCULATION WITH LIVE RABIES VIRUS VACCINE

Persons inadvertently inoculated with the Flury strain vaccine are not considered at risk, and antirabies prophylaxis is not indicated. No information is available by which to judge risk from accidental inoculation of other attenuated strains in veterinary use.

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